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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,684	07/03/2003	MacKlin Brian Arnold	X-12150A	7313

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ELI LILLY AND COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS, IN 46206-6288

EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/613,684	Macklin Brian Arnold et al.	
	Examiner	Art Unit	
	Janet L Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-10,14-16,18 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-5,7-10 and 14* is/are allowed.

6)☒ Claim(s) *15,17,18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/744,412.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-10, 14-16, 18, and 20 pending in the instant application.

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 35 U.S.C. 120/121 is acknowledged. The instant application is a divisional of U.S. Application No. 09/744,412, filed January 23, 2001, now allowed, which is a 371 of PCT/US99/17126 filed July 28, 1999, which claims priority to U.S. Provisional Application No. 60/094,997 filed July 31, 1998.

Information Disclosure Statement

2. Receipt is acknowledged of Applicants' Information Disclosure Statement (IDS), filed July 3, 2003, which has been considered by the Examiner. Please refer to the signed copies of the PTO-1449 forms submitted herewith.

Election/Restrictions

3. Receipt is acknowledged of Applicants' Preliminary Amendment, submitted July 3, 2003, which has been reviewed by the Examiner and entered of record in the file. Pursuant to the restriction requirement in the parent, U.S. Appl. No. 09/744,412, Applicants have amended the instant claims to prosecute the invention of Group I, drawn to phenyl-thiophenes containing no additional heterocyclic ring of any kind and composition thereof.

4. Accordingly, claims 1, 7-10, 14, 16, 18, and 20 have been amended in order to delete the non-elected subject matter, and claims 6, 11, 17, 19, and 21 have been cancelled.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 16 rejected under 35 U.S.C. 112, first paragraph, as being a reach-through claim. The claim is directed to a method of potentiating glutamate receptor function in a mammal, yet these claims do not meet the requirements for "how to use" under 35 U.S.C. 112, first paragraph, and 35 U.S.C. 101, as stated below. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth below, one skilled in the art clearly would not know how to use the claimed invention. The claim is directed to the mechanism for the potentiating activity, yet the claim fails to present a tangible use. The Examiner suggests claiming the possible uses, rather than claiming the mechanism, which is speculative.

7. Claims 18 and 20 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While the various diseases/disorders may be listed on page 9 of the specification, the "laundry list" of diseases and conditions encompassed by claims 18 and 20 are not enabled. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the claims are directed to many diseases that are not enabled in the specification, including those recited in claims 18 and 20.

The nature of the invention

The nature of the invention is of methods of treating many different unrelated diseases or conditions, comprising administering the instant claimed compound to a patient in need thereof.

The state of the prior art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. Furthermore, the diseases recited within claims 18 and 20 are not the same but different diseases. By definition, treating ADHD requires the use of stimulant medications, while diseases such as movement disorders and age-induced memory impairment are not encompassed by this definition and are completely unrelated. Such as psychotic patients require administering antipsychotics, on the other hand, treating depression employs the use of anti-depressants such as SSRIs.

The predictability or lack thereof in the art

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of claim 1 and the increased response of the glutamate receptor, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1.

The amount of direction or guidance present

The specification has enabled only the compounds according to claim 1 that selectively

potentiate glutamate receptor-mediated response. Furthermore, treatment of the claimed distinct diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating the symptoms of attention disorders such as ADHD (inattention, hyperactivity, and impulsivity) would not employ the same methods as treating memory loss. The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

The presence or absence of working examples

The data provided in the disclosure is insufficient evidence for methods of treating all claimed diseases. In fact, the only disclosure in the specification at all is found on pages 30-32 wherein an ELISA assay is described, wherein glutamate-evoked efflux of calcium into GluR4B transfected HEK293 cells is measured. In view of the diversified multiple diseases as claimed, such few universal disclosures fails to provide specific description in guiding one skilled in the art to pick and choose the specific compounds that would be useful for treating one or a specific group of pathological conditions. The standard of 35 USC 112, first paragraph rejections is that the application *itself* must inform, rather than direct, others to find out for themselves, please see *In re Garnder*, 166 USPQ 138.

The breadth of the claims

Applicants are claiming methods of treating a broad number of diseases that are unrelated. The argument that the diseases claimed by the Applicants are all treated by potentiating the glutamate receptor is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the claimed diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every unrelated disease/condition encompassed by claims 18 and 20, using the instant claimed compounds. One of skill in the art would need to determine what listed diseases would be benefited by the potentiating the glutamate receptor and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the diseases by said potentiating.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of all recited diseases in claims 18 and 20. As a result, necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 is indefinite because the amount of compound present in the composition is unspecified, and it is not clear from the claim itself as to the amount of compound that Applicants are intending to claim. The Examiner suggests adding the phrase, "a therapeutically effective amount of" after the term "comprises" in line 1 of the claim.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claim 16 rejected under 35 U.S.C. 101 as being a reach-through claim, because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The claimed method of potentiating glutamate receptor function in a mammal does not comply with the utility requirement since there is no disclosed pharmaceutical use, i.e. a method of treating a response "mediated by the glutamate receptor" is not equivalent to a positive recitation of how to use the product for the treatment of a particular disease of real world relevance. The Examiner suggests incorporating some of the specific diseases that Applicants are enabled for treating, from the specification, or canceling the claims in view of the remaining method claims.

Conclusion

12. In conclusion, compound claims 1-5, 7-10, and 14 are free of the prior art and appear to be in condition for allowance. Claims 15, 16, 18, and 20 stand rejected.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
September 17, 2004

for Kamal Saeed
Joseph K. McKane
Supervisory Patent Examiner, Art Unit 1626